REMARKS

Claims 12 to 14 have been amended. Claims 1 to 3, 7 to 14, 23 to 25, and 57 to 59 are pending and under consideration.

The amendments to claims 12 to 14 merely add the phrase "isolated host cell" to the claims. Support for those amendments is found in the specification, e.g., at page 22, line 2, to page 23, line 4. Thus, the amendments add no new matter.

Rejection of Claims 57 to 59 under 35 U.S.C. § 112, first paragaraph (Written Description)

The Examiner rejected claims 57 to 59 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. See the Action at pages 2 to 3. Specifically, the Examiner alleged that claims 57 to 59 "are directed to all possible polynucleotides encoding an archaeal replication factor A ("RFA") possessing 95% identity to SEQ ID NO: 66. The specification, however, only provides a single representative species having the nucleic acid sequence of SEQ ID NO: 65, encompassed by these claims." See id. at page 3. The Examiner then alleged that "[t]he specification also fails to describe additional representative species of these polynucleotides by any identifying structural characteristics or properties other than that recited in claim 57, for which no predictability of function is apparent. It is unclear what, if any functions are associated with the encoded 'archael replication factor A' proteins of the claimed polynucleotides." See id. The Examiner then concludes that "Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and

exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention." Applicants respectfully traverse.

"The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species ... by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." MPEP § 2163 at 2100-174.

Claim 57 recites:

> 57. An isolated an purified polynucleotide encoding an archaeal replication factor A ("RFA") comprising: (a) a polynucelotide comprising the nucleotide sequence set forth in Figure 16 (SEQ ID NO: 65) or the nucleotide sequence of Figure 16 starting with nucleotide 7; (b) a polynucleotide encoding an amino acid sequence comprising the amino acid sequence set forth in Figure 17 (SEQ ID NO: 66) or the amino acid sequence of Figure 17 starting with amino acid 3; or (c) a polynucleotide encoding an amino acid sequence possessing 95% identity to SEQ ID NO: 66.

Claims 58 and 59 depend from claim 57.

The Examiner alleged that "[t]here is no disclosure of any particular structure to function/activity relationship in the single species." See Action at page 3. Applicants assert that a disclosure of such a relationship is not required to satisfy the written description requirement in this case. Rather, as emphasized by the Federal Circuit in *Enzo Biochem. v. Gen-Probe Inc.*, when a claim recites only functional characteristics, that claim may still be adequately described when those functional characteristics are coupled with a known or disclosed correlation between function and structure. 296 F.3d

1316, 1324 (Fed. Cir. 2002). That situation arises, for example, when claiming an antibody that binds to antigen X, as discussed in Example 16 of the "Synopsis of Application of Written Description Guidelines" (Synopsis; available at http://www.uspto.gov/web/menu/ written.pdf), which is cited in the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. § 112, paragraph 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1101 (January 5, 2001). Example 16 explains that a hypothetical claim to an "isolated antibody capable of binding to antigen X" is adequately described *even though it does not recite any specific structure* for the claimed antibodies, because of the known correlation between antibody structure and function. That is, a known correlation between structure and function supports a finding of adequate written description for a claim that recites only function.

In addition, the MPEP states that "[a] biomolecule sequence described **only** by a functional characteristic, *without any known or disclosed correlation between that function and the structure* of the sequence, normally is not a sufficient identifying characteristic." MPEP § 2163, page 2100-174 (emphasis added). That is, a known or disclosed correlation between function and structure may rescue a claim that recites only functional characteristics from a finding of inadequate written description. Nowhere does the MPEP state, however, that a known correlation between function and structure is required where a claim recites both specific structure and function.

The present claims recite both specific structure and function. First, the claimed polynucleotides comprise specific structure. Specifically, the language "a polynucleotide encoding an amino acid sequence possessing 95% identity to SEQ ID NO: 66" clearly conveys specific structure of the claimed polynucleotides. Second, the

claimed polynucleotides have specific function. The claimed polynucleotides encode an "archaeal replication factor A." As explained in the specification, an archaeal replication factor A has certain functions and activities that can enhance a polymerization reaction. See the specification, e.g., at page 5, lines 12 to 13, which discusses "single-stranded DNA binding proteins (RFA) that bind and stabilize the resulting single-stranded DNA template.... " Thus, applicants have provided structural and functional characteristics sufficient to describe the claimed genus of isolated polynucleotides.

Applicants assert that the situation described in Example 16 of the Synopsis, in which the Office relies on a known correlation between structure and function in order to find adequate written description for a claim reciting only functional characteristics, does not apply to this case. Rather, the present claims are more closely analogous to Example 9 of the Synopsis.

Example 9 of the Synopsis discusses a hypothetical claim reciting an "isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity." Synopsis at pages 35 to 36. Like the present claims, the hypothetical claim of Example 9 recites both specific structure and function. Nowhere in the analysis of Example 9 does the Office rely on any known or disclosed correlation between structure and function in finding that the hypothetical claim is adequately described. Rather, the Synopsis states that

> [A] person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim **yield structurally**

> **similar DNAs. Thus, a representative number of species is disclosed**, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the invention.

Id. at pages 36-37 (emphasis added).

Like the hypothetical claim in Example 9, the instant claim 57 recites isolated structurally similar polynucleotides. The hypothetical claim in Example 9 uses hybridization conditions to define the polynucleotides of the genus. In contrast, instant claim 57 uses percent identity to define the polynucleotides of the genus. Applicants assert, however, that the language "a polynucleotide encoding an amino acid sequence possessing 95% identity to SEQ ID NO: 66" would encompass structurally similar polynucleotides similar to the structurally similar polynucleotides encompassed by using "highly stringent hybridization" language in a claim. Stated another way, applicants assert that the polynucleotides encompassed by a claim that includes "highly stringent hybridization" language would include polynucleotides encoding an amino acid sequence with 95% identity to the amino acid sequence encoded by the reference polynucleotide used in the hybridization. Thus, applicants assert that, under the guidelines of the Synopsis, Applicants were in possession of the genus of claim 57.

Finally, applicants enclose a copy of a decision of the Board of Patent Appeals and Interferences, which supports applicants' assertion that a known or disclosed correlation between structure and function is not required for a finding of adequate written description of a claim that recites both structure and function. *See* Decision on Appeal, *Ex parte Chung et al.*, Appeal No. 2004-2201 (Bd. Pat. App. Int. 2004)

(*Chung*).[1] In that case, under the written description requirement, the Examiner had rejected a claim reciting an isolated nucleic acid that has 60% identity and hybridizes under specific conditions to a specific polynucleotide, and which encodes an mRNA that is expressed in a particular tissue. *Chung* at page 2. In reversing the Examiner and finding the claim adequately described, the Board relied heavily on the similarities between the claim at issue and Example 9 of the Synopsis. *Id.* at pages 4 to 7. Furthermore, the Board admonished the Examiner for insisting, without basis, that an adequate written description requires that the function recited in claim 1 be coupled to the structure of the claimed genus. *Id.* at page 6 ("The examiner states that the functional characteristic recited in claim 1 is 'uncoupled with the structure of the claim genus,' Examiner's Answer, page 9, but does not explain why that is significant in determining whether claim 1 complies with the written description analysis.").

While *Chung* is nonprecedential, it is strongly indicative of the Board's unwillingness to allow Examiners to expand the written description requirements beyond those articulated by the Federal Circuit and the USPTO's published guidelines.

In view of the above remarks, applicants respectfully request reconsideration and withdrawal of the written description rejection of claims 57 to 59 under 35 U.S.C. § 112, first paragraph.

[1] While that case is not binding precedent, it provides evidence of the Board's favorable view of Example 9 of the Synopsis.

Rejection of Claims 12, 14, and 57 under 35 U.S.C. § 112, first paragaraph (Enablement)

The Examiner rejected claims 12, 14, and 57 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. See the Action at pages 3 to 7. Applicants will address the rejection of claim 57 separately from the rejection of claims 12 and 14.

With regard to claim 57, the Examiner alleged that "[c]laim 57 is so broad as to encompass any polynucleotide encoding an archael replication factor A, having 95% identity to SEQ ID NO:66." See Action at page 4. The Examiner alleged that "[t]he claims... do not place any functional limits on the enzymes encoded by the claimed polynucleotides." See id. The Examiner then goes on to state:

> the specification does not establish: (A) regions of the encoded protein structure which may be modified without effecting the desired activity/function; (B) the general tolerance of the encoded protein (SEQ ID NO: 66) to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of any protein having a similar function as SEQ ID NO: 66, with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Id. at page 5. The Examiner then cites Ngo et al., *Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox,* The Protein Folding Problem and Tertiary Structure Prediction, Birkhauser, Boston MA pp433 and 492 to 495 (1994) ("Ngo") to attempt to support the proposition that "the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable...." See id. at page 6. The Examiner concludes that "it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotide analogs of the claimed genus." See id. Applicants respectfully traverse.

"The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt,* 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (CCPA 1976)." *See* MPEP §2164.01. As noted in *In re Wands,* 858 F2d 731, (Fed. Cir. (1988)), "[e]nablement is not precluded by the necessity for some experimentation such as routine screening." *See Wands* at 736-37.

At the outset, applicants note that the Examiner takes two contradictory positions in the rejection. On the one hand, the Examiner alleged that "[t]he claims... do not place any functional limits on the enzymes encoded by the claimed polynucleotides." See id. at page 4. The Examiner made a similar allegation in the written description rejection, stating "[i]t is unclear what, if any functions are associated with the encoded 'archael replication factor A' proteins of the claimed polynucloetides." See id. at page 3. On the other hand, the Examiner goes on to allege that the claims are not enabled because the specification does not provide "a rational and predictable scheme for modifying any amino acid residue of any protein having a similar *function* as SEQ ID NO: 66, with an expectation of obtaining the desired biological *function*...." See id. at page 5 (emphasis added). The claim either possess functional elements or it does not. In this case, for the reasons cited above in response to the written description rejection, applicants assert that the claimed polynucleotides have specific function. The claimed polynucleotides encode an "archaeal replication factor A." As explained in the specification, an archaeal replication factor A has certain functions and activities that can enhance a polymerization reaction. See the specification, e.g., at page 5, lines 12 to 13.

In the rejection, the Examiner also cites Ngo to attempt to support his allegation that the relationship between the sequence of a peptide and its tertiary structure is not well understood and is not predictable. See Action at page 6. Ngo discusses algorithms for taking an amino acid sequence and predicting its structure using only its amino acid sequence. See, e.g., Ngo at page 492, which states "[i]t is not known whether there exists an efficient algorithm for predicting the structure of a given protein *from its amino acid sequence alone*." (Emphasis added.) In this case, however, one skilled in the art would not be trying to determine the structure of a given protein from its amino acid sequence alone. Instead, one would be trying to determine whether a particular amino acid change in an amino acid sequence would cause the protein encoded by that amino acid sequence to cease to function as an RFA. Those are two different inquiries. And even if one can't predict the structure of a given protein using only its amino acid sequence, that does not render completely unpredictable the question of whether a change to a particular known amino acid sequence would cause a protein to lack a particular function.

In fact, predicting the structure of a protein from an amino acid sequence was only one of the tools available to those of skill in the art to determine if a particular amino acid change would cause a protein to cease to function. As the Examiner concedes, recombinant and mutagenesis techniques were known. See Action at page 5. Such techniques would have included knowledge of how to make conservative amino acid substitutions, e.g., replacing a hydrophobic amino acid in a sequence with a different hydrophobic amino acid. Such techniques would also have included knowledge of how to align related proteins to identify conserved regions in the amino

acid sequences, and non-conserved regions where amino acid changes are more likely to be tolerated without impacting the function of the resulting protein.

Furthermore, even if one skilled in the art could not have predicted whether a particular amino acid change would cause an RFA to cease to function, applicants have provided extensive guidance and two separate assays which can be used to screen an RFA for function. Specifically, gel shift experiments are described in Example 18, which describe how one of skill in the art could test a putative RFA for single stranded DNA binding activity. Additionally, Figures 19 to 21 describe amplification reactions, which describe how one of skill in the art could test a putative RFA for its ability to enhance the yield or specificity of an amplification reaction. Applicants assert that any particular RFA could be screened in a day using one of those experimental protocols and that those experiments do not rise to the level of undue experimentation. For comparison, the MPEP provides an example of reasonable experimentation wherein studies that cost $50,000 and took six to twelve months failed to show undue experimentation. See MPEP § 2164.06(I).

Thus, applicants assert that claim 57 is enabled.

With regard to claims 12 and 14, the Examiner alleged that "[c]laims 12 and 14 are so broad as to encompass any recombinant cell comprising the vector of claim 7. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to those cells, which are not isolated and may be part of a transgenic organism or tissue." See Action at page 6. With regard to claim 14, the Examiner alleged, "applicants provide no examples or guidance enabling the generation of those cells that are not isolated (i.e. transgenic tissues or organisms)." See id.

Solely to expedite prosecution and without acquiescing to the rejection, applicants have amended claims 12 to 14 to include the language "isolated host cell.' Those amendments should obviate the Examiner's rejection.

Applicants respectfully request reconsideration and withdrawal of the enablement rejections of claims 12, 14, and 57 under 35 U.S.C. § 112, first paragraph.

Applicants respectfully submit that the application is in condition for allowance. In the event the Examiner does not find the claims allowable, applicants request that the Examiner contact the undersigned at (650) 849-6658 to set up an interview.

Please grant any extensions of time required to enter this response, and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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